AM100012OX1

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: MARK ET AL.

Application No.: 09/425,501

Filed: October 22, 1999

For: PABLO, A POLYPEPTIDE THAT INTERACTS WITH BCL-XL AND USES RELATED THERETO

Examiner: S. Chunduru

Group Art Unit: 1656

November 1, 2002

The Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. §1.132

Sir:

I, Robert Mark, declare the following in support of the above-identified application.

1. I hold a Ph.D. from the University of Kentucky School of Medicine with a major emphasis on Anatomy and Neurobiology. I also hold a B.S. in Biotechnology from the Rochester Institute of Technology.

2. I currently serve as a Senior Research Scientist at Wyeth where I work on research and development in the Neurosciences Therapeutic Area. I

have previously worked on numerous gene discovery programs for multiple therapeutic indications.

3. I am a member of the Society for Neuroscience.

4. Because of my work, and my involvement in the Society for Neuroscience, I am very knowledgeable regarding the current literature, theory, and recent developments relating to molecular neurosciences and apoptosis-related genes.

5. I am quite familiar with U.S. Patents, and in performing my duties as a scientist, I have analyzed and scientifically evaluated numerous patents.

6. Exhibit A and Exhibit B were obtained from a Blast search (ncbi.nlm.nih.gov/blast) of SEQ ID NO:1 and SEQ ID NO:2 respectively.

7. Based on the attached Blast search (Exhibit A, pages 17-19), and excluding Nagase and subsequent references relating to Nagase, the nucleotide species most analogous to SEQ ID NO:1 of the present invention comes from the mouse (listed as gi|18542418|gb|AF467773.1|), which has 91% sequence identity to SEQ ID NO:1. See also Benachenhou, N. et al, "Characterization and expression analyses of the mouse Wiskott-Aldrich syndrome protein (WASP)

family member Wave1/Scar," Gene, 290 (2002) 131-140.

8. Based on the attached Blast search (Exhibit B, page 6), and excluding Nagase and subsequent references relating to Nagase, the protein sequence most analogous to SEQ ID NO:2 of the present invention comes from the mouse (listed as gi|13994209|ref|NP_114083.1|). This has 98% identity with the total sequence. The 98% sequence identity in claim 65 is a claim of appropriate breadth, which is necessary for the protection of the invention against those who would copy it by making insubstantial changes.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application or any patent issuing thereon.

Robert J. Mark

Robert J. Mark, Ph.D.
Senior Research Scientist

NOTARY

State of New Jersey }
ss: Monmouth Junction
Middlesex County }

On the 4th day of November 2002, Robert Mark personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that she executed the same, of her own free will and for the purposes set forth.

ELIZABETH BACKER MELICK
NOTARY PUBLIC OF NEW JERSEY
MY COMMISSION EXPIRES APRIL 4, 2006

Elizabeth Backer Melick

AM100012

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)
: Examiner: S. Chunduru
MARK ET AL.)
: Group Art Unit: 1656
Application No.: 09/425,501)
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Filed: October 22, 1999)
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For: PABLO, A POLYPEPTIDE)
THAT INTERACTS WITH :
BCL-XL, AND USES RELATED)
THERETO : March 1, 2002

The Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

I, Brad Ozenberger, declare the following in support of the above-identified application.

1. I hold a Ph.D. from the University of Missouri School of Medicine in with a major emphasis on Molecular Biology. I also hold a B.S. in Biology from the University of Missouri.

2. I currently serve as a Principal Research Scientist at Wyeth-Ayerst Research (a division of American Home Products Corporation) where I work on research and development in the Neurosciences Therapeutic Area. I have previously worked on

numerous gene discovery programs for multiple therapeutic indications.

3. I am a member of the American Association for the Advancement of Science and the Society for Neuroscience.

4. Because of my work, and my involvement in the Society for Neuroscience, I am very knowledgeable regarding the current literature, theory and recent developments relating to molecular neurosciences and apoptosis-related genes.

5. I am quite familiar with U.S. Patents, and I am named as inventor on eleven issued US patents and several patent applications. In performing my duties as a scientist, I have analyzed and scientifically evaluated numerous patents.

6. I am submitting this declaration on behalf of the assignee of the instant application in order to present proof of the novelty of the claimed invention relative to Nagase et al. (DNA Res., 3:321-329, 1996) hereinafter "Nagase" (Exhibit A).

7. I am familiar with the prosecution history of this patent application, having read in particular the specification, the present claims, and the Examiner's position regarding the prior art, as set forth in the Office Action dated June 28, 2001

(Exhibit B).

8. In order to compare the current invention to Nagase and in particular, to determine whether Nagase anticipates the current invention, I reviewed Nagase in light of my own knowledge of the state of the art relating to apoptosis and the molecular biology of neurons. Specifically, I reviewed Nagase in order to determine if that publication contains an enabling disclosure of the current invention.

9. The Examiner alleges that Nagase teaches the coding sequence of a cDNA clone from human myeloid cell line KG-1 and brain, wherein Nagase discloses a cDNA clone which is identical or [containing] absolute homology (100%) to the claimed sequences in SEQ ID Nos. 1 and 2 of the instant invention (see Exhibit B at page 4). The Examiner further alleges that Nagase discloses that the cDNA clones showed homology to genes that play key roles in regulation of developmental stages, apoptosis and cell-to-cell interaction.

10. As revealed by a careful reading of Nagase, the Examiner misstates the disclosure of Nagase.

11. The Nagase publication discloses a sequencing effort of human cDNA clones which attempted to identify as yet unidentified human genes. The effort managed to identify the sequences of 80 clones; and

the predicted coding sequences of the corresponding genes were designated KIAA0201 to KIAA0280.

10. The Examiner's assertion is based on the abstract which states:

> Computer search against the public databases indicated that ...58 genes carried sequences which show some similarities to known genes. Protein motifs that matched those in the PROSITE motif database were found in 25 genes and significant transmembrane domains were identified in 30 genes. Among the known genes to which significant similarity was shown, the genes that play key roles in regulation of developmental stages, apoptosis and cell-to-cell interaction were included. Abstract, emphasis added.

11. However, this is nothing more than a general statement, with no correlation between the 80 predicted coding sequences and functional, cellular activity of the encoded proteins. In fact, the cDNA clone designated KIAA0269, which is alleged to anticipate SEQ ID NO:1 of the invention, is suggested by Nagase to be most closely homologous (29.9%) to an extensin-like protein from *Zea mays* (see Exhibit A, Table 1). *Zea mays* is a species of corn. Tissue expression of KIAA0269 was observed in kidney, pancreas, thymus, testis, ovary, small intestine, colon, peripheral blood leukocytes and brain (Exhibit A, Table 3).

12. Table 2 of Nagase demonstrated that the

predicted sequence of KIAA0269 contained no known motifs or significant transmembrane domains.

13. Thus, there is nothing disclosed or described in Nagase suggesting that a protein encoded by the sequence of KIAA0269 would play a key role in regulation of developmental stages, apoptosis or cell-to-cell interaction. Indeed, Nagase did not reveal any use for the KIAA0269 sequence or a protein encoded by that sequence. Further, Nagase did not disclose how to use KIAA0269 or the protein encoded by that sequence.

14. Based on my knowledge of the state of the relevant art, no known method of using KIAA0269 or the protein encoded by that sequence existed prior to the present invention which discloses that the protein designated PABLO may be used to modulate BCL-XL in neurons.

15. Nagase merely discloses the primary structure of an unknown cDNA, but failed to enable any method of using the cDNA or the protein that sequence was predicted to encode.

16. These observations lead me to conclude that Nagase did not put the public in possession of the instant invention.

11. Further, Nagase failed to anticipate the present

invention because Nagase failed to provide an enabling disclosure.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application or any patent issuing thereon.

Brad Ozenberger

Brad Ozenberger, Ph.D.
Principal Research Scientist

NOTARY

State of New Jersey }
County of Middlesex } ss:

On the 1st day of March 2002, Brad Ozenberger personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he executed the same, of his own free will and for the purposes set forth.

Marilyn Winkler

MARILYN WINKLER
NOTARY PUBLIC OF NEW JERSEY
MY COMMISSION EXPIRES 1/25/2007

BEFORE THE OFFICE OF ENROLLMENT AND DISCIPLINE
UNITED STATE PATENT AND TRADEMARK OFFICE

LIMITED RECOGNITION UNDER 37 CFR § 10.9(b)

Gavin Bogle is hereby given limited recognition under 37 CFR §10.9(b) as an employee of Wyeth-Ayerst, to prepare and prosecute patent applications wherein the assignee of record of the entire interest is American Home Products Corporation, Wyeth-Ayerst Laboratories, Wyeth-Ayerst International, Inc., Wyeth-Ayerst Research, or Genetics Institute. This limited recognition shall expire on the date appearing below, or when whichever of the following events first occurs prior to the date appearing below: (i) Gavin Bogle ceases to lawfully reside in the United States, (ii) Gavin Bogle's employment with Wyeth-Ayerst ceases or is terminated, or (iii) Gavin Bogle ceases to remain or reside in the United States on an H-1B visa.

This document constitutes proof of such recognition. The original of this document is on file in the Office of Enrollment and Discipline of the U.S. Patent and Trademark Office.

Expires: July 9, 2003

Harry I. Moatz
Director of Enrollment and Discipline